Cannabinoid Wikibook

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Run From the Cure

Run From the Cure	
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Editing by	Christain Laurette
Running time	58 min
Country	

Run From the Cure is a documentary film about the medical uses of cannabis. More specifically the use of "Hemp Oil" or Cannabis Oil. Which is a cocktail of many cannabinoids. Primarily in hemp are Tetrahydrocannabinoland [1] and (CBD). [2] This film claims that with the use of this substance, can treat many diseases and medical conditions.[3]

References

[1] http://en.wikipedia.org/wiki/Cannabinoid#Tetrahydrocannabinol|
[2] http://en.wikipedia.org/wiki/Cannabidiol|Cannabidiol
[3] http://phoenixtears.ca/what-it-does-and-how-it-works/

Hash oil

Hash oil is a resinous matrix of cannabinoids produced by a solvent extraction of cannabis. Hash oil is a concentrated product with a high THC content, which generally varies between 40% and 90%.[1] Related **honey oil** is a specific type of hash oil extracted with butane. Hash oil is traditionally a dark, golden hue.[2][3]

Closeup image of a drop of **hash oil** on the end of a needle.

Usage

Hash oil can be consumed in various ways, including smoking, vaporization, or may be consumed orally.[4]

Solvents

- Butane (boiling point ~−0.5 °C (**unknown operator: u'strong'** °F)[5]): One of the most common solvents used. Hash oil extracted with butane is often referred to as "butane honey oil", or "BHO" by the marijuana using community.
- Isopropanol (Rubbing alcohol) (usually 70% isopropyl alcohol and 30% water) (boiling point ~82 °C (**unknown operator: u'strong'** °F)[6]): One of the most common solvents used. Cannabis oil extracted with isopropanol is sometimes referred to as "Iso Oil". The advantages of isopropyl alcohol are that it is commonly available, cheap, and is somewhat less toxic and explosive than is methanol. Unfortunately, because it contains water, many of the water-soluble, non-psychoactive substances are also extracted. The oil yield using rubbing alcohol is twice that of methanol, and is proportionally less potent. Water-soluble components may also give the oil undesirable taste and burning qualities. If the oil is to be re-extracted later with a more selective solvent, however, it matters little what it is like at this point. Once most of the alcohol is evaporated, the water & remaining isopropyl alcohol that was in the solvent remains with the oil.
- Methyl alcohol (also known as methanol or wood alcohol) (boiling point 64.7 °C (**unknown operator: u'strong'** °F)[7]): This solvent is also commonly employed. Methanol is available at many pharmacies and in larger quantities at industrial chemical supply companies. Methanol is toxic and explosive. Inhalation of fumes makes one sick and even small amounts may cause permanent damage. Any traces of the solvent remaining in the oil product will be hazardous to the consumer. Methanol evaporates at approximately 65 °C (**unknown operator: u'strong'** °F) and does not extract a lot of the water-soluble component.
- Ethanol (also known as ethyl alcohol or grain alcohol) (boiling point 78 °C (**unknown operator: u'strong'** °F)): This is a very desirable solvent. It has extraction properties very similar to methanol, but is not as toxic.Denatured alcohol is composed of ethanol with added poison, to deter ingestion and to avoid taxes on beverage alcohol. Depending on what type of poison is used to create the denatured alcohol, the poison may or may not be effectively removed by evaporation. However, denatured alcohol is more widely available and cheaper than poison-free ethanol.
- Petroleum ether (boiling point 30 °C (**unknown operator: u'strong'** °F)[8] —60 °C (**unknown operator: u'strong'** °F)[9]): Petroleum ether is a light solvent that is much more selective than any of the alcohols. Extracting with petroleum ether produces an oil that is twice as potent by weight as oil extracted with alcohol. The cannabis material may be extracted directly with petroleum ether but, due to petroleum ether's highly

explosive nature, the oil is usually first removed from the plant material with alcohol and then re-extracted with petroleum ether. This requires a much smaller amount of the dangerous solvent. Petroleum ether is available at hardware stores in many countries, including the US. Petroleum ether should not be confused with diethyl ether, the term "ether" alone more commonly refers to diethyl ether.

- Acetone Boiling point 57 °C (**unknown operator: u'strong'** °F) Easily available as a solvent and degreaser, Acetone evaporates rapidly and is probably the safest solvent used in health terms. Acetone has been studied extensively and is generally recognized to have low acute and chronic toxicity if ingested and/or inhaled. Acetone has been rated as a GRAS (Generally Recognized as Safe) substance for food use and is produced and disposed of in the human body through normal metabolic processes. The most hazardous property of acetone is its extreme flammability. At temperatures greater than acetone's flash point of −20 °C (−4 °F), air mixtures of between 2.5% and 12.8% acetone, by volume, may explode or cause a flash fire. Vapors can flow along surfaces to distant ignition sources and flash back.

Dangers

There are a wide variety of dangers associated with use of chemical solvents. The most common danger is from flammability. Structure fires and severe burns have been caused when production accidents occur.[10]

Images

Hash oil

Honey oil

Golden cannabis oil

Honey oil

Butane honey oil evaporating

References

[1] "Bulletin on Narcotics - 1980 Issue 4 - 005" (http://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1980-01-01_4_page006.html), *UNODC*, , retrieved 2012-03-10

[2] King, Leslie A. (2003). *The Misuse of Drugs Act*. Royal Society of Chemistry. pp. 75–76. ISBN 978-0-85404-625-6.

[3] Mamakind (December 4, 2003), *Honey oil made easy* (http://www.cannabisculture.com/v2/articles/3083.html), Cannabis Culture Magazine, , retrieved 2 May 2011

[4] Cynthia Kuhn, Scott Swartzwelder, Wilkie Wilson, Leigh Heather Wilson, Jeremy Foster (2003). *Buzzed*. W. W. Norton & Company; 2 Rev Upd edition. pp. 139–140. ISBN 978-0-393-32493-8.

[5] "Butane 99%" (http://www.sigmaaldrich.com/catalog/product/aldrich/494402?lang=en&region=US). Sigma-Aldrich. . Retrieved 2012-03-29.

[6] "2-Propanol 70% in H2O" (http://www.sigmaaldrich.com/catalog/product/sial/563935?lang=en&region=US). Sigma-Aldrich. .

[7] "Methanol CHROMASolv® Plus, for HPLC, ≥99.9% CH3OH" (http://www.sigmaaldrich.com/catalog/product/sial/646377?lang=en&region=US). Sigma-Aldrich. . Retrieved 2012-03-29.

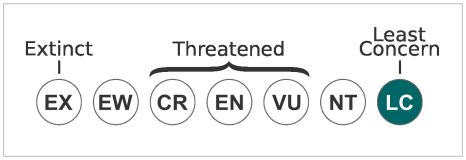
[8] "Petroleum ether puriss. p.a., low boiling, bp 30-40 °C" (http://www.sigmaaldrich.com/catalog/product/sial/77399?lang=en&region=US). Sigma-Aldrich. . Retrieved 2012-03-29.
[9] "Petroleum ether puriss. p.a., high boiling, bp 60-80 °C" (http://www.sigmaaldrich.com/catalog/product/sial/32248?lang=en&region=US). Sigma-Aldrich. . Retrieved 2012-03-29.
[10] Reverend Damuzi (September 13, 2004), *Hash oil explosions* (http://www.cannabisculture.com/articles/3518.html), Cannabis Culture Magazine, , retrieved 2 May 2011

External links

- Erowid: Honey Oil Butane Extraction Tips (http://www.erowid.org/plants/cannabis/cannabis_info22.shtml)
- (http://www.marijuana.com/news/2012/03/dab-life-a-brief-and-wondrous-history-of-concentrates/)

Cannabis

Cannabis

Common hemp
Conservation status

Least Concern (IUCN 3.1)
Scientific classification
Kingdom: — Plantae
(unranked): — Angiosperms
(unranked): — Eudicots
(unranked): — Rosids
Order: — Rosales
Family: — Cannabaceae
Genus: — ***Cannabis*** L.
Species
Cannabis sativa L.[1] *Cannabis indica* Lam. (putative)[1] *Cannabis ruderalis* Janisch. (putative)

Cannabis (/ˈkænəbɪs/; *Cán-na-bis*) is a genus of flowering plants that includes three putative varieties, *Cannabis sativa*,[1] *Cannabis indica*,[1] and *Cannabis ruderalis*. These three taxa are indigenous to Central Asia, and South Asia.[2] *Cannabis* has long been used for fibre (hemp), for seed and seed oils, for medicinal purposes, and as a recreational drug. Industrial hemp products are made from *Cannabis* plants selected to produce an abundance of fiber. To satisfy the UN Narcotics Convention, some *Cannabis* strains have been bred to produce minimal levels of

THC, the principal psychoactive constituent responsible for the "high" associated with marijuana. Marijuana consists of the dried flowers of *Cannabis* plants selectively bred to produce high levels of THC and other psychoactive cannabinoids. Various extracts including hashish and hash oil are also produced from the plant.[3]

Etymology

The word *cannabis* is from Greek κάνναβις (*kánnabis*) (see Latin *cannabis*),[4] which was originally Scythian or Thracian.[5] It is related to the Persian *kanab*, the English *canvas* and possibly even to the English *hemp* (Old English hænep).[5] In modern Hebrew, קַנַּבּוֹס *qannabōs* modern pronunciation: Hebrew pronunciation: [kanaˈbos] is used but מַעֲלֶה עָשָׁן *maʿăleh ʿāšān* modern pronunciation: Hebrew pronunciation: [ma.aˈle aˈʃan] (smoke bringer) is the ancient term. Old Akkadian *qunnabtu*, Neo-Assyrian and Neo-Babylonian *qunnabu* were used to refer to the plant meaning "a way to produce smoke."[6][7][8]

Description

Cannabis is an annual, dioecious, flowering herb. The leaves are palmately compound or digitate, with serrate leaflets.[9] The first pair of leaves usually have a single leaflet, the number gradually increasing up to a maximum of about thirteen leaflets per leaf (usually seven or nine), depending on variety and growing conditions. At the top of a flowering plant, this number again diminishes to a single leaflet per leaf. The lower leaf pairs usually occur in an opposite leaf arrangement and the upper leaf pairs in an alternate arrangement on the main stem of a mature plant.

Underside of *Cannabis sativa* leaf, showing diagnostic venation

The leaves have a peculiar and diagnostic venation pattern that enables persons poorly familiar with the plant to distinguish a *Cannabis* leaf from unrelated species that have confusingly similar leaves (see illustration). As is common in serrated leaves, each serration has a central vein extending to its tip. However,the serration vein originates from lower down the central vein of the leaflet, typically opposite to the position of, not the first notch down, but the next notch. This means that on its way from the midrib of the leaflet to the point of the serration, the vein serving the tip of the serration passes close by the intervening notch. Sometimes the vein will actually pass tangent to the notch, but often it will pass by at a small distance, and when that happens a spur vein (occasionally a pair of such spur veins) branches off and joins the leaf margin at the deepest point of the notch. This venation pattern varies slightly among varieties, but in general it enables one to tell *Cannabis* leaves from superficially similar leaves without difficulty and without special equipment. Tiny samples of *Cannabis* plants also can be identified with precision by microscopic examination of leaf cells and similar features, but that requires special expertise and equipment.[10]

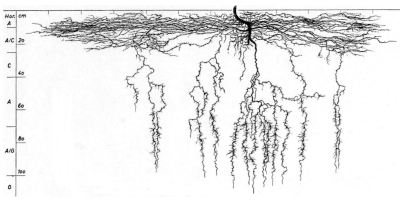
Cannabis normally has imperfect flowers, with staminate "male" and pistillate "female" flowers occurring on separate plants.[11] It is not unusual, however, for individual plants to bear both male and female flowers.[12] Although monoecious plants are often referred to as "hermaphrodites," true hermaphrodites (which are less common) bear staminate and pistillate structures on individual flowers, whereas monoecious plants bear male and female flowers at different locations on the same plant. Male flowers are normally borne on loose panicles, and female flowers are borne on racemes.[13] "At a very early period the Chinese recognized the *Cannabis* plant as dioecious,"[14] and the (ca. 3rd century BCE) *Erya* dictionary defined *xi* 枲 "male *Cannabis*" and *fu* 莩 (or *ju* 苴) "female *Cannabis*".[15]

Cannabis is growing like weeds at the foot of Dhaulagiri.

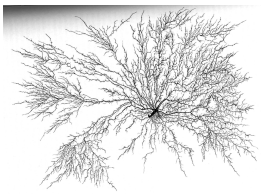
All known strains of *Cannabis* are wind-pollinated[16] and produce "seeds" that are technically achenes.[17] Most strains of *Cannabis* are short day plants,[16] with the possible exception of *C. sativa* subsp. *sativa* var. *spontanea* (= *C. ruderalis*), which is commonly described as "auto-flowering" and may be day-neutral.

Cannabis, like many organisms, is diploid, having a chromosome complement of 2n=20, although polyploid individuals have been artificially produced.[18] The first genome sequence of *Cannabis*, which is estimated to be 820 Mb in size, was published in 2011 by a team of Canadian scientists.[19] The plant is believed to have originated in the mountainous regions northwest of the Himalayas. It is also known as hemp, although this term is often used to refer only to varieties of *Cannabis* cultivated for non-drug use. *Cannabis* plants produce a group of chemicals called cannabinoids, which produce mental and physical effects when consumed.

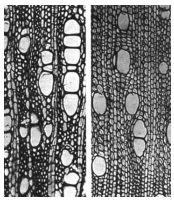
Cannabinoids, terpenoids, and other compounds are secreted by glandular trichomes that occur most abundantly on the floral calyxes and bracts of female plants.[20] As a drug it usually comes in the form of dried flower buds (marijuana), resin (hashish), or various extracts collectively known as hashish oil.[3] In the early 20th century, it became illegal in most of the world to cultivate or possess *Cannabis* for sale or personal use.



Root system side view



Root system top view



Micrograph sativa (left), indica (right)

Taxonomy

The genus *Cannabis* was formerly placed in the Nettle (Urticaceae) or Mulberry (Moraceae) family, and later, along with the *Humulus* genus (hops), in a separate family, the Hemp family (Cannabaceae sensu stricto).[21] Recent phylogenetic studies based on cpDNA restriction site analysis and gene sequencing strongly suggest that the Cannabaceae sensu stricto arose from within the former Celtidaceae family, and that the two families should be merged to form a single monophyletic family, the Cannabaceae sensu lato.[22][23]

Cannabis sativa leaf, dorsal aspect

Various types of *Cannabis* have been described, and variously classified as species, subspecies, or varieties:[24]

- plants cultivated for fiber and seed production, described as low-intoxicant, non-drug, or fiber types.
- plants cultivated for drug production, described as high-intoxicant or drug types.
- escaped, hybridised, or wild forms of either of the above types.

Cannabis plants produce a unique family of terpeno-phenolic compounds called cannabinoids, which produce the "high" one experiences from consuming marijuana. The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and/or Δ^9-tetrahydrocannabinol (THC), but only THC is psychoactive. Since the early 1970s, *Cannabis* plants have been categorized by their chemical phenotype or "chemotype," based on the overall amount of THC produced, and on the ratio of THC to CBD.[25] Although overall cannabinoid production is influenced by environmental factors, the THC/CBD ratio is genetically determined and remains fixed throughout the life of a plant.[26] Non-drug plants produce relatively low levels of THC and high levels of CBD, while drug plants produce high levels of THC and low levels of CBD. When plants of these two chemotypes cross-pollinate, the plants in the first filial (F_1) generation have an intermediate chemotype and produce similar amounts of CBD and THC. Female plants of this chemotype may produce enough THC to be utilized for drug production.[25][27]

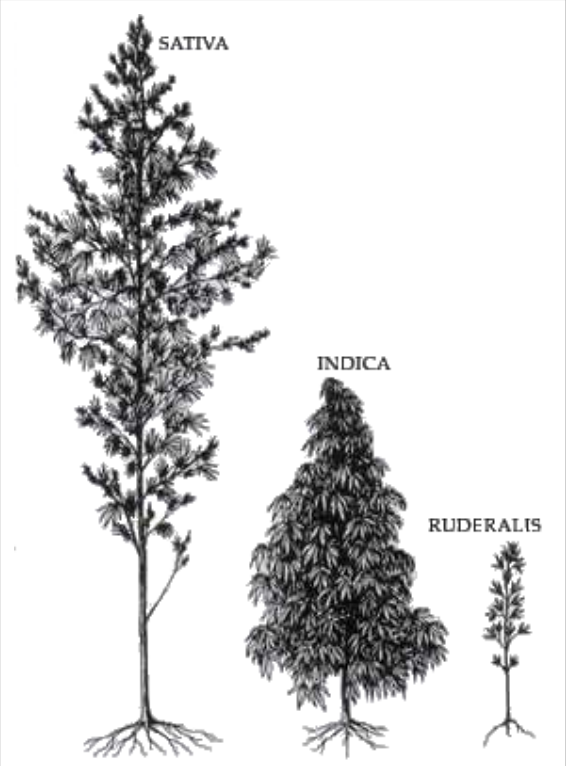
Top of *Cannabis* plant in vegetative growth stage

Whether the drug and non-drug, cultivated and wild types of *Cannabis* constitute a single, highly variable species, or the genus is polytypic with more than one species, has been a subject of debate for well over two centuries. This is a contentious issue because there is no universally accepted definition of a species.[28] One widely applied criterion for species recognition is that species are "groups of actually or potentially interbreeding natural populations which are reproductively isolated from other such groups."[29] Populations that are physiologically capable of interbreeding, but morphologically or genetically divergent and isolated by geography or ecology, are sometimes considered to be separate species.[29] Physiological barriers to reproduction are not known to occur within *Cannabis*, and plants from widely divergent sources are interfertile.[18] However, physical barriers to gene exchange (such as the Himalayan mountain range) might have enabled *Cannabis* gene pools to diverge before the onset of human intervention, resulting in speciation.[30] It remains controversial whether sufficient morphological and genetic divergence occurs within the genus as a result of geographical or ecological isolation to justify recognition of more than one species.[31][32][33]

Difference between *Cannabis indica* and *Cannabis sativa*

Cannabis indica may have a CBD:THC ratio 4–5 times that of *Cannabis sativa*. Cannabis strains with relatively high CBD:THC ratios are less likely to induce anxiety than vice versa. This may be due to CBD's antagonistic effects at the cannabinoid receptors, compared to THC's partial agonist effect. CBD is also a 5-HT_{1A} receptor agonist, which may also contribute to an anxiolytic effect.[34] This likely means the high concentrations of CBD found in *Cannabis indica* mitigate the anxiogenic effect of THC significantly.[34] The effects of *sativa* are well known for its cerebral high, hence used daytime as medical cannabis, while *indica* are well known for its sedative effects and preferred night time as medical cannabis.[34]

Early classifications



Relative size of varieties of *Cannabis*

The *Cannabis* genus was first classified using the "modern" system of taxonomic nomenclature by Carolus Linnaeus in 1753, who devised the system still in use for the naming of species.[35] He considered the genus to be monotypic, having just a single species that he named *Cannabis sativa* L. (L. stands for Linnaeus, and indicates the authority who first named the species). Linnaeus was familiar with European hemp, which was widely cultivated at the time. In 1785, noted evolutionary biologist Jean-Baptiste de Lamarck published a description of a second species of *Cannabis*, which he named *Cannabis indica* Lam.[36] Lamarck based his description of the newly named species on plant specimens collected in India. He described *C. indica* as having poorer fiber quality than *C. sativa*, but greater utility as an inebriant. Additional *Cannabis* species were proposed in the 19th century, including strains from China and Vietnam (Indo-China) assigned the names *Cannabis chinensis* Delile, and *Cannabis gigantea* Delile ex Vilmorin.[37] However, many taxonomists found these putative species difficult to distinguish. In the early 20th century, the single-species concept was still widely accepted, except in the Soviet Union where *Cannabis* continued to be the subject of active taxonomic study. The name *Cannabis indica* was listed in various Pharmacopoeias, and was widely used to designate *Cannabis* suitable for the manufacture of medicinal preparations.[38]

20th century


Cannabis ruderalis

In 1924, Russian botanist D.E. Janichevsky concluded that ruderal *Cannabis* in central Russia is either a variety of *C. sativa* or a separate species, and proposed *C. sativa* L. var. *ruderalis* Janisch. and *Cannabis ruderalis* Janisch. as alternative names.[24] In 1929, renowned plant explorer Nikolai Vavilov assigned wild or feral populations of *Cannabis* in Afghanistan to *C. indica* Lam. var. *kafiristanica* Vav., and ruderal populations in Europe to *C. sativa* L. var. *spontanea* Vav.[27][37] In 1940, Russian botanists Serebriakova and Sizov proposed a complex classification in which they also recognized *C. sativa* and *C. indica* as separate species. Within *C. sativa* they recognized two subspecies: *C. sativa* L. subsp. *culta* Serebr. (consisting of cultivated plants), and *C. sativa* L. subsp. *spontanea* (Vav.) Serebr. (consisting of wild or feral plants). Serebriakova and Sizov split the two *C. sativa* subspecies into 13 varieties, including four distinct groups within subspecies *culta*. However, they did not divide *C. indica* into subspecies or varieties.[24][39] This excessive splitting of *C. sativa* proved too unwieldy, and never gained many adherents.

In the 1970s, the taxonomic classification of *Cannabis* took on added significance in North America. Laws prohibiting *Cannabis* in the United States and Canada specifically named products of *C. sativa* as prohibited materials. Enterprising attorneys for the defense in a few drug busts argued that the seized *Cannabis* material may

not have been *C. sativa*, and was therefore not prohibited by law. Attorneys on both sides recruited botanists to provide expert testimony. Among those testifying for the prosecution was Dr. Ernest Small, while Dr. Richard E. Schultes and others testified for the defense. The botanists engaged in heated debate (outside of court), and both camps impugned the other's integrity.[31][32] The defense attorneys were not often successful in winning their case, because the intent of the law was clear.[40]

In 1976, Canadian botanist Ernest Small[41] and American taxonomist Arthur Cronquist published a taxonomic revision that recognizes a single species of *Cannabis* with two subspecies: *C. sativa* L. subsp. *sativa*, and *C. sativa* L. subsp. *indica* (Lam.) Small & Cronq.[37] The authors hypothesized that the two subspecies diverged primarily as a result of human selection; *C. sativa* subsp. *sativa* was presumably selected for traits that enhance fiber or seed production, whereas *C. sativa* subsp. *indica* was primarily selected for drug production. Within these two subspecies, Small and Cronquist described *C. sativa* L. subsp. *sativa* var. *spontanea* Vav. as a wild or escaped variety of low-intoxicant *Cannabis*, and *C. sativa* subsp. *indica* var. *kafiristanica* (Vav.) Small & Cronq. as a wild or escaped variety of the high-intoxicant type. This classification was based on several factors including interfertility, chromosome uniformity, chemotype, and numerical analysis of phenotypic characters.[25][37][42]

Professors William Emboden, Loran Anderson, and Harvard botanist Richard E. Schultes and coworkers also conducted taxonomic studies of *Cannabis* in the 1970s, and concluded that stable morphological differences exist that support recognition of at least three species, *C. sativa*, *C. indica*, and *C. ruderalis*.[43][44][45][46] For Schultes, this was a reversal of his previous interpretation that *Cannabis* is monotypic, with only a single species.[47] According to Schultes' and Anderson's descriptions, *C. sativa* is tall and laxly branched with relatively narrow leaflets, *C. indica* is shorter, conical in shape, and has relatively wide leaflets, and *C. ruderalis* is short, branchless, and grows wild in central Asia. This taxonomic interpretation was embraced by *Cannabis* aficionados who commonly distinguish narrow-leafed "sativa" drug strains from wide-leafed "indica" drug strains.[48]

Continuing research

Molecular analytical techniques developed in the late 20th century are being applied to questions of taxonomic classification. This has resulted in many reclassifications based on evolutionary systematics. Several studies of Random Amplified Polymorphic DNA (RAPD) and other types of genetic markers have been conducted on drug and fiber strains of *Cannabis*, primarily for plant breeding and forensic purposes.[49][50][51][52][53] Dutch *Cannabis* researcher E.P.M. de Meijer and coworkers described some of their RAPD studies as showing an "extremely high" degree of genetic polymorphism between and within populations, suggesting a high degree of potential variation for selection, even in heavily selected hemp cultivars.[26] They also commented that these analyses confirm the continuity of the *Cannabis* gene pool throughout the studied accessions, and provide further confirmation that the genus comprises a single species, although theirs was not a systematic study *per se*.

Karl W. Hillig, a graduate student in the laboratory of long-time *Cannabis* researcher Paul G. Mahlberg[54] at Indiana University, conducted a systematic investigation of genetic, morphological, and chemotaxonomic variation among 157 *Cannabis* accessions of known geographic origin, including fiber, drug, and feral populations. In 2004, Hillig and Mahlberg published a chemotaxomic analysis of cannabinoid variation in their *Cannabis* germplasm collection. They used gas chromatography to determine cannabinoid content and to infer allele frequencies of the gene that controls CBD and THC production within the studied populations, and concluded that the patterns of cannabinoid variation support recognition of *C. sativa* and *C. indica* as separate species, but not *C. ruderalis*.[27] The authors assigned fiber/seed landraces and feral populations from Europe, central Asia, and Asia Minor to *C. sativa*. Narrow-leaflet and wide-leaflet drug accessions, southern and eastern Asian hemp accessions, and feral Himalayan populations were assigned to *C. indica*. In 2005, Hillig published a genetic analysis of the same set of accessions (this paper was the first in the series, but was delayed in publication), and proposed a three-species classification, recognizing *C. sativa*, *C. indica*, and (tentatively) *C. ruderalis*.[30] In his doctoral dissertation published the same year, Hillig stated that principal components analysis of phenotypic (morphological) traits failed to differentiate the

putative species, but that canonical variates analysis resulted in a high degree of discrimination of the putative species and infraspecific taxa.[55] Another paper in the series on chemotaxonomic variation in the terpenoid content of the essential oil of *Cannabis* revealed that several wide-leaflet drug strains in the collection had relatively high levels of certain sesquiterpene alcohols, including guaiol and isomers of eudesmol, that set them apart from the other putative taxa.[56] Hillig concluded that the patterns of genetic, morphological, and chemotaxonomic variation support recognition of *C. sativa* and *C. indica* as separate species. He also concluded there is little support to treat *C. ruderalis* as a separate species from *C. sativa* at this time, but more research on wild and weedy populations is needed because they were underrepresented in their collection.

In September 2005, New Scientist reported that researchers at the Canberra Institute of Technology had identified a new type of *Cannabis* based on analysis of mitochondrial and chloroplast DNA.[57] The New Scientist story, which was picked up by many news agencies and web sites, indicated that the research was to be published in the journal *Forensic Science International*.[58]

Popular usage

The scientific debate regarding taxonomy has had little effect on the terminology in widespread use among cultivators and users of drug-type *Cannabis*. *Cannabis* aficionados recognize three distinct types based on such factors as morphology, native range, aroma, and subjective psychoactive characteristics. "Sativa" is the term used to describe the most widespread variety, which is usually tall, laxly branched, and found in warm lowland regions. "Indica" is used to designate shorter, bushier plants adapted to cooler climates and highland environments. "Ruderalis" is the term used to describe the short plants that grow wild in Europe and central Asia.

Breeders, seed companies, and cultivators of drug type *Cannabis* often describe the ancestry or gross phenotypic characteristics of cultivars by categorizing them as "pure indica," "mostly indica," "indica/sativa," "mostly sativa", or "pure sativa."

One of the most popular and potent sativas in Africa is Malawi Gold, locally known as *chamba*. It is internationally known for its potency and its flavor.

Reproduction

Breeding systems

Cannabis is predominantly dioecious,[16][59] although many monoecious varieties have been described.[60] Subdioecy (the occurrence of monoecious individuals and dioecious individuals within the same population) is widespread.[61][62][63] Many populations have been described as sexually labile.[51][64][65]

Cannabis sativa fruits (achenes) that contain the seeds.

Cannabis flower with visible trichomes.

Male *Cannabis* flower buds.

As a result of intensive selection in cultivation, *Cannabis* exhibits many sexual phenotypes that can be described in terms of the ratio of female to male flowers occurring in the individual, or typical in the cultivar.[66] Dioecious varieties are preferred for drug production, where typically the female flowers are used. Dioecious varieties are also preferred for textile fiber production, whereas monoecious varieties are preferred for pulp and paper production. It has been suggested that the presence of monoecy can be used to differentiate licit crops of monoecious hemp from illicit drug crops.[61] However, *sativa* strains often produce monoecious individuals, probably as a result of inbreeding.

Mechanisms of sex determination

Cannabis has been described as having one of the most complicated mechanisms of sex determination among the dioecious plants.[66] Many models have been proposed to explain sex determination in *Cannabis*.

Based on studies of sex reversal in hemp, it was first reported by K. Hirata in 1924 that an XY sex-determination system is present.[64] At the time, the XY system was the only known system of sex determination. The X:A system was first described in Drosophila spp in 1925.[67] Soon thereafter, Schaffner disputed Hirata's interpretation,[68] and published results from his own studies of sex reversal in hemp, concluding that an X:A system was in use and that furthermore sex was strongly influenced by environmental conditions.[65]

Since then, many different types of sex determination systems have been discovered, particularly in plants.[59] Dioecy is relatively uncommon in the plant kingdom, and a very low percentage of dioecious plant species have been determined to use the XY system. In most cases where the XY system is found it is believed to have evolved recently and independently.[69]

Since the 1920s, a number of sex determination models have been proposed for *Cannabis*. Ainsworth describes sex determination in the genus as using "an X/autosome dosage type".[59]

A male hemp plant.

Dense raceme of carpellate flowers typical of drug-type varieties of *Cannabis*.

The question of whether heteromorphic sex chromosomes are indeed present is most conveniently answered if such chromosomes were clearly visible in a karyotype. *Cannabis* was one of the first plant species to be karyotyped; however, this was in a period when karyotype preparation was primitive by modern standards (see History of Cytogenetics). Heteromorphic sex chromosomes were reported to occur in staminate individuals of dioecious "Kentucky" hemp, but were not found in pistillate individuals of the same variety. Dioecious "Kentucky" hemp was assumed to use an XY mechanism. Heterosomes were not observed in analyzed individuals of monoecious "Kentucky" hemp, nor in an unidentified German cultivar. These varieties were assumed to have sex chromosome composition XX.[70] According to other researchers, no modern karyotype of *Cannabis* had been published as of 1996.[71] Proponents of the XY system state that Y chromosome is slightly larger than the X, but difficult to differentiate cytologically.[72]

More recently, Sakamoto and various co-authors[73][74] have used RAPD to isolate several genetic marker sequences that they name Male-Associated DNA in *Cannabis* (MADC), and which they interpret as indirect evidence of a male chromosome. Several other research groups have reported identification of male-associated markers using RAPD and AFLP.[75][76][77] Ainsworth commented on these findings, stating,

> "It is not surprising that male-associated markers are relatively abundant. In dioecious plants where sex chromosomes have not been identified, markers for maleness indicate either the presence of sex chromosomes which have not been distinguished by cytological methods or that the marker is tightly linked to a gene involved in sex determination.[59] "

Environmental sex determination is known to occur in a variety of species.[78] Many researchers have suggested that sex in *Cannabis* is determined or strongly influenced by environmental factors.[65] Ainsworth reviews that treatment with auxin and ethylene have feminizing effects, and that treatment with cytokinins and gibberellins have masculinizing effects.[59] It has been reported that sex can be reversed in *Cannabis* using chemical treatment.[79] A PCR-based method for the detection of female-associated DNA polymorphisms by genotyping has been developed.[80]

Industrial and personal uses

Cannabis is used for a wide variety of purposes.

Hemp

Cannabis sativa stem longitudinal section

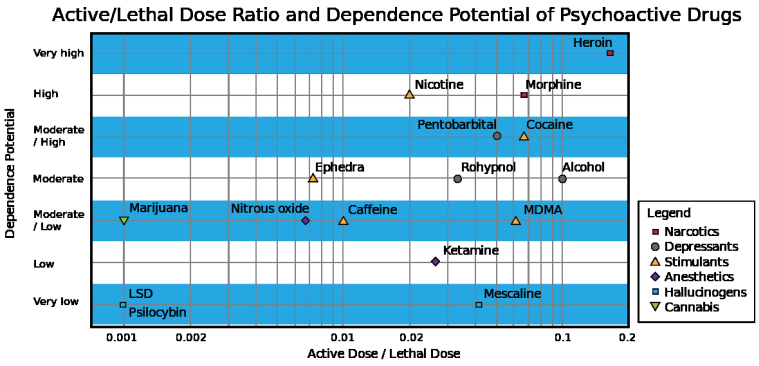
Hemp is the durable soft fiber from the stalk of *Cannabis* sativa plants. Certain varieties may grow more than six metres tall. Cannabis plants used for hemp production are not suitable for most traditional recreational uses, because such plants produce minimal levels of the major psychoactive compounds (THC in particular). Traditional strains of *Cannabis* plants cultivated for drug production tend to be difficult to camouflage among hemp plants, because they are visibly different.[81]

Hemp producers sell hemp seeds as a health food, as they are rich in sought-after essential fatty acids and have a good amino acid balance, together with various vitamins and minerals. Hemp "milk" is a milk substitute made from hemp seeds; it is both dairy- and gluten-free.[82]

As a field crop hemp is fairly undemanding and matures more rapidly than most.[83] Horticulturally hemp plants have attractions such as requiring little application of insecticide because they are little attacked; they also do not require much application of herbicides because they grow competitively, with good height, density and foliage. Such characteristics make it easy to grow hemp without excessive environmental impact as long as the application of fertilizer is competently managed. The world's leading producer of hemp is China.[84]

Hemp is valuable in tens of thousands of commercial products, especially as fibre[81] ranging from paper, cordage, construction material and textiles in general, to clothing, in which hemp is stronger and longer-lasting than cotton. It also is a useful source of biofuels (from the oils found in the seeds) and medical products. Hemp has been used by many civilizations, from China to Europe (and later North America) during the last 12,000 years or so.[81][85] In modern times novel applications and improvements have been explored with modest commercial success.[86][87]

Recreational use



Comparison of physical harm and dependence regarding various drugs.[88]

Cannabis is a popular recreational drug around the world, only behind alcohol, caffeine and tobacco. In the United States alone, it is believed that over 100 million Americans have tried Cannabis, with 25 million Americans having used it within the past year.[89]

The psychoactive effects of Cannabis are known to have a biphasic nature. Primary psychoactive effects include a state of relaxation, and to a lesser degree, euphoria from its main psychoactive compound, tetrahydrocannabinol. Secondary psychoactive effects, such as a facility for philosophical thinking, introspection and metacognition have been reported amongst cases of anxiety and paranoia.[90] Finally, the tertiary psychoactive effects of the drug cannabis, can include an increase in heart rate and hunger, believed to be

caused by 11-OH-THC, a psychoactive metabolite of THC produced in the liver.

Normal cognition is restored after approximately three hours for larger doses via a smoking pipe, bong or vaporizer.[90] However, if a large amount is taken orally the effects may last much longer. After 24 hours to a few days, minuscule psychoactive effects may be felt, depending on dosage, frequency and tolerance to the drug.

Cannabis Museum in Amsterdam.

Various forms of the drug cannabis exist, including extracts such as hashish and hash oil[3] which, because of appearance, are more susceptible to adulterants when left unregulated.

The plant *Cannabis sativa* is known to cause more of a "high" by stimulating hunger and by producing a rather more comedic, or energetic feeling. Conversely, the *Cannabis indica* plant is known to cause more of a "stoned" or meditative feeling, possibly because of a higher THC to CBD ratio.[91]

Cannabidiol (CBD), which has no psychotropic effects by itself[92] (although sometimes showing a small stimulant effect, similar to caffeine), attenuates, or reduces[93] the higher anxiety levels caused by THC alone.[94]

According to the UK medical journal *The Lancet*, Cannabis has a lower rate of dependence compared to both nicotine and alcohol.[95] However, everyday use of Cannabis can in some cases be correlated with psychological withdrawal symptoms such as irritability and insomnia,[90] and evidence could suggest that if a user experiences stress, the likeliness of getting a panic attack increases because of an increase of THC metabolites.[96][97] However, Cannabis withdrawal symptoms are typically mild and are never life-threatening.[95]

Medical use

A synthetic form of the main psychoactive cannabinoid in *Cannabis*, Δ^9-tetrahydrocannabinol (THC), is used as a treatment for a wide range of medical conditions.[98]

In the United States, although the Food and Drug Administration (FDA) does acknowledge that "there has been considerable interest in its use for the treatment of a number of conditions, including glaucoma, AIDS wasting, neuropathic pain, treatment of spasticity associated with multiple sclerosis, and chemotherapy-induced nausea," the agency has not approved "medical marijuana". There are currently 2 oral forms of cannabis (cannabinoids) available by prescription in the United States for nausea and vomiting associated with cancer chemotherapy: dronabinol (Marinol) and nabilone (Cesamet). Dronabinol is also approved for the treatment of anorexia associated with AIDS.[99] The FDA does facilitate scientific investigations into the medical uses of cannabinoids.[100]

In a collection of writings on medical marijuana by 45 researchers, a literature review on the medicinal uses of *Cannabis* and cannabinoids concluded that established uses include easing of nausea and vomiting, anorexia, and weight loss; "well-confirmed effect" was found in the treatment of spasticity, painful conditions (i.e. neurogenic pain), movement disorders, asthma, and glaucoma. Reported but "less-confirmed" effects included treatment of allergies, inflammation, infection, epilepsy, depression, bipolar disorders, anxiety disorder, dependency and withdrawal. Basic level research was being carried out at the time on autoimmune disease, cancer, neuroprotection, fever, and disorders of blood pressure.[101]

Clinical trials conducted by the American Marijuana Policy Project, have shown the efficacy of cannabis as a treatment for cancer and AIDS patients, who often suffer from clinical depression, and from nausea and resulting weight loss due to chemotherapy and other aggressive treatments.[102] A synthetic version of the cannabinoid THC named dronabinol has been shown to relieve symptoms of anorexia and reduce agitation in elderly Alzheimer's patients.[103] Dronabinol has been approved for use with anorexia in patients with HIV/AIDS and chemotherapy-related nausea. This drug, while demonstrating the effectiveness of *Cannabis* at combating several disorders, is more expensive and less available than whole cannabis and has not been shown to be effective or

safe.[104]

Glaucoma, a condition of increased pressure within the eyeball causing gradual loss of sight, can be treated with medical marijuana to decrease this intraocular pressure. There has been debate for 25 years on the subject. Some studies have shown a reduction of IOP in glaucoma patients who smoke cannabis,[105] but the effects are generally short-lived. There exists some concern over its use since it can also decrease blood flow to the optic nerve. Marijuana lowers IOP by acting on a cannabinoid receptor on the ciliary body called the CB receptor.[106] Although *Cannabis* may not be the best therapeutic choice for glaucoma patients, it may lead researchers to more effective treatments. A promising study shows that agents targeted to ocular CB receptors can reduce IOP in glaucoma patients who have failed other therapies.[107]

Medical cannabis is also used for analgesia, or pain relief. It is also reported to be beneficial for treating certain neurological illnesses such as epilepsy, and bipolar disorder.[75] Case reports have found that *Cannabis* can relieve tics in people with obsessive compulsive disorder and Tourette syndrome. Patients treated with tetrahydrocannabinol, the main psychoactive chemical found in *Cannabis*, reported a significant decrease in both motor and vocal tics, some of 50% or more.[108][109][110] Some decrease in obsessive-compulsive behavior was also found.[108] A recent study has also concluded that cannabinoids found in *Cannabis* might have the ability to prevent Alzheimer's disease.[111] THC has been shown to reduce arterial blockages.[112]

Another potential use for medical cannabis is movement disorders. *Cannabis* is frequently reported to reduce the muscle spasms associated with multiple sclerosis; this has been acknowledged by the Institute of Medicine, but it noted that these abundant anecdotal reports are not well-supported by clinical data. Evidence from animal studies suggests that there is a possible role for cannabinoids in the treatment of certain types of epileptic seizures.[113] A synthetic version of the major active compound in *Cannabis*, THC, is available in capsule form as the prescription drug dronabinol (Marinol) in many countries. The prescription drug Sativex, an extract of cannabis administered as a sublingual spray, has been approved in Canada for the treatment of multiple sclerosis.[114]

Cannabis was manufactured and sold by U.S. pharmaceutical companies from the 1880s through the 1930s, but the lack of documented information on the frequency and effectiveness of its use makes it difficult to evaluate its medicinal value in these forms. Cannabis was listed in the *1929–1930 Physicians' Catalog of the Pharmaceutical and Biological Products of Parke, Davis & Company* as an active ingredient in ten products for cough, colic, neuralgia, cholera mordus and other medical conditions, as well as a "narcotic, analgesic, and sedative."[115] The *1929–1930 Physicians' Catalog* also lists compound medications containing cannabis that in some cases were apparently formulated by medical doctors, in its "Pills and Tablets" section.[116]

As cannabis is further legalized for medicinal use, it is possible that some of the foregoing compound medicines, whose formulas have been copied exactly as published, may be scientifically tested to determine whether they are effective medications. Writing in the Canadian Medical Association Journal, smoking cannabis from a pipe may significantly relieve chronic pain in patients with damaged nerves.[117] A study on New Zealand support the claim that that long-term cannabis smoking increases the risk of lung cancer in young adults.[118]

Ancient and religious uses

The Yanghai Tombs, a vast ancient cemetery (54 000 m^2) situated in the Turfan district of the Xinjiang Uyghur Autonomous Region of the People's Republic of China, have revealed the 2700-year-old grave of a shaman. He is thought to have belonged to the Jushi culture recorded in the area centuries later in the *Hanshu*, Chap 96B.[119] Near the head and foot of the shaman was a large leather basket and wooden bowl filled with 789g of cannabis, superbly preserved by climatic and burial conditions. An international team demonstrated that this material contained tetrahydrocannabinol, the psychoactive component of cannabis. The cannabis was presumably employed by this culture as a medicinal or psychoactive agent, or an aid to divination. This is the oldest documentation of cannabis as a pharmacologically active agent.[120]

Settlements which date from *c*. 2200-1700 BCE in the Bactria and Margiana contained elaborate ritual structures with rooms containing everything needed for making drinks containing extracts from poppy (opium), hemp (cannabis), and ephedra (which contains ephedrine).[121]

> "While we have no evidence of the use of ephedra among the steppe tribes, we have already seen that they did share in the cultic use of hemp, a practice that ranged from Romania east to the Yenisei River from at least the 3rd millenium BC onwards where its use was later encountered in the apparatus for smoking hemp found at Pazyryk."[122]

Cannabis is first referred to in Hindu Vedas between 2000 and 1400 BCE, in the *Atharvaveda*. By the 10th century CE, it has been suggested that it was referred to by some in India as "food of the gods".[123] Cannabis use eventually became a ritual part of the Hindu festival of Holi.

In Buddhism, cannabis is generally regarded as an intoxicant and therefore a hindrance to development of meditation and clear awareness. In ancient Germanic culture, *Cannabis* was associated with the Norse love goddess, Freya.[124][125] An anointing oil mentioned in Exodus is, by some translators, said to contain *Cannabis*.[126] Sufis have used *Cannabis* in a spiritual context since the 13th century CE.[127]

In the Punjab, Cannabis or Sukha (ਸੁੱਖਾ ਪ੍ਰਰਸਾਦ), "peace-giver", is the term Sikhs use to refer to it. Initiated by the tenth guru of the Sikhs, Guru Gobind Singh, cannabis or bhang (ਭੰਗ) was used to help in meditation and was also used before battles to aid as a painkiller, growing naturally all over Punjab. Narrated by many historical and native accounts cannabis is pounded by the Sikhs, especially during religious festivals like Hola Mohalla.[43] Even today, Nihang Sikhs gather in their thousands at Anandpur, on the occasion of the festival of Hola Mohalla and display their martial skills and of course cannabis is pounded by the Nihang Sikhs. This tradition has been in place since the time of Guru Gobind Singh. Their fighting style is referred to as shastar vidiya, which is among the most intimidating and brutal martial art. The compositions from the Sri Dasam Granth are used in unison with the battle maneuvers.
In modern times the Rastafari movement has embraced *Cannabis* as a sacrament.[128] Elders of the Ethiopian Zion Coptic Church, a religious movement founded in the United States in 1975 with no ties to either Ethiopia or the Coptic Church, consider *Cannabis* to be the Eucharist, claiming it as an oral tradition from Ethiopia dating back to the time of Christ.[129] Like the Rastafari, some modern Gnostic Christian sects have asserted that *Cannabis* is the Tree of Life.[130][131] Other organized religions founded in the 20th century that treat *Cannabis* as a sacrament are the THC Ministry,[132] the Way of Infinite Harmony, Cantheism,[133] the Cannabis Assembly[134] and the Church of Cognizance.

Rastafari and Sikh use tend to be among the biggest consumers of modern Cannabis use.

Aspects of *cannabis* production and use

- Cannabis cultivation discusses aspects of cultivation for medicinal and recreational drug purposes.
- Cannabis (drug) discusses its use as a recreational drug.
- Health issues and the effects of cannabis discusses the pharmacology, physical, and mental effects of *Cannabis* when used as drug.
- Hemp discusses its uses as a source of housing, oil, food, fibers, and industrial materials.
- Legality of cannabis focuses on the law and enforcement aspects of growing, transporting, selling and using *Cannabis* as a drug.
  - Cannabis reclassification in the United Kingdom.
  - Cannabis rescheduling in the United States.

A *cannabis* field.

  - Drug policy of the Netherlands.
- Medical Cannabis discusses its use as a medication.
- Spiritual use of cannabis discusses sacramental and religious use.

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External links

- International Plant Names Index (IPNI) (http://www.ipni.org/ipni/advPlantNameSearch.do?find_family=&find_genus=Cannabis&find_species=&find_infrafamily=&find_infragenus=&find_infraspecies=&find_authorAbbrev=&find_includePublicationAuthors=off&find_includeBasionymAuthors=off&find_publicationTitle=&find_isAPNIRecord=on&find_isAPNIRecord=false&find_isGCIRecord=on&find_isGCIRecord=false&find_isIKRecord=on&find_isIKRecord=false&find_rankToReturn=all&output_format=normal&find_sortByFamily=on&find_sortByFamily=off&query_type=by_query&back_page=plantsearch)
- The Endocannabinoid System Network (ECSN) (http://www.endocannabinoid.net/) - Contains medical information to the Endocannabinoid System
- Erowid: Cannabis (Marijuana) Vault (http://www.erowid.org/plants/cannabis/)
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Cannabinoid

Cannabinoids are a class of diverse chemical compounds that activate cannabinoid receptors. These include the endocannabinoids (produced naturally in the body by humans and animals),[1] the phytocannabinoids(found in cannabis and some other plants), and synthetic cannabinoids (produced chemically by humans). The most notable cannabinoid is the phytocannabinoid Δ^9-tetrahydrocannabinol (THC), the primary psychoactive compound of cannabis.[2][3] However, there are known to exist numerous other cannabinoids with varied effects.

Synthetic cannabinoids encompass a variety of distinct chemical classes: the classical cannabinoids structurally related to THC, the nonclassical cannabinoids (cannabimimetics) including the aminoalkylindoles, 1,5-diarylpyrazoles, quinolines, and arylsulphonamides, as well as eicosanoids related to the endocannabinoids.[2]

Cannabinoid receptors

Before the 1980s, it was often speculated that cannabinoids produced their physiological and behavioral effects via nonspecific interaction with cell membranes, instead of interacting with specific membrane-bound receptors. The discovery of the first cannabinoid receptors in the 1980s helped to resolve this debate. These receptors are common in animals, and have been found in mammals, birds, fish, and reptiles. At present, there are two known types of cannabinoid receptors, termed CB_1 and CB_2,[1] with mounting evidence of more.[4] The human brain has more cannabinoid receptors than any other GPCR type.[5]

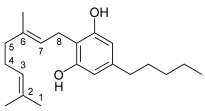
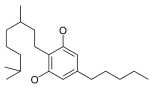
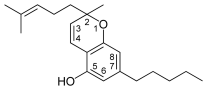
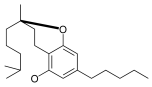
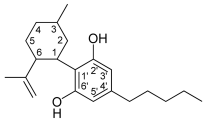
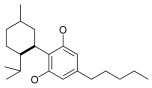
Cannabinoid receptor type 1

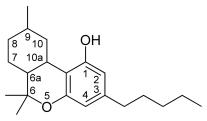
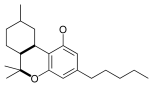
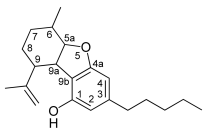
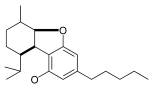
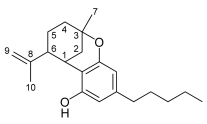
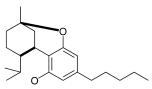
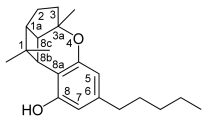
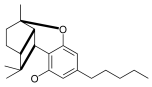
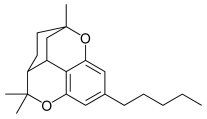
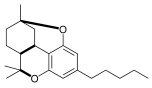
CB_1 receptors are found primarily in the brain, to be specific in the basal ganglia and in the limbic system, including the hippocampus.[1] They are also found in the cerebellum and in both male and female reproductive systems. CB_1 receptors are absent in the medulla oblongata, the part of the brain stem responsible for respiratory and cardiovascular functions. Thus, there is not the risk of respiratory or cardiovascular failure that can be produced by some drugs. CB_1 receptors appear to be responsible for the euphoric and anticonvulsive effects of cannabis.

Cannabinoid receptor type 2

CB_2 receptors are predominantly found in the immune system, or immune-derived cells[6] with the greatest density in the spleen. While found only in the peripheral nervous system, a report does indicate that CB_2 is expressed by a subpopulation of microglia in the human cerebellum .[7] CB_2 receptors appear to be responsible for the anti-inflammatory and possibly other therapeutic effects of cannabis.[6]

Phytocannabinoids

Type	Skeleton	Cyclization
Cannabigerol-type **CBG**		
Cannabichromene-type **CBC**		
Cannabidiol-type **CBD**		

Tetrahydrocannabinol- and Cannabinol-type **THC, CBN**		
Cannabielsoin-type **CBE**		
iso-Tetrahydrocannabinol-type ***iso*-THC**		
Cannabicyclol-type **CBL**		
Cannabicitran-type **CBT**		
Main classes of natural cannabinoids		

Phytocannabinoids (also called *natural cannabinoids*, *herbal cannabinoids*, and *classical cannabinoids*) are known to occur in several different plant species. These include *Cannabis sativa*, *Cannabis indica*, *Echinacea purpurea*, *Echinacea angustifolia*, *Echinacea pallida*, *Acmella oleracea*, *Helichrysum umbraculigerum*, and *Radula marginata*.[8] The best known herbal cannabinoids are Δ9-tetrahydrocannabinol (THC) from *Cannabis* and the lipophilic alkamides (alkylamides) from *Echinacea* species.[8]

A significant number of cannabinoids are found in both *Cannabis* and *Echinacea* plants. In *Cannabis*, these cannabinoids are concentrated in a viscous resin produced in structures known as glandular trichomes. In *Echinacea* species, cannabinoids are found throughout the plant structure, but are most concentrated in the roots and stems.[9] Tea (Camellia sinensis) catechins have an affinity for human cannabinoid receptors.[10]

Phytocannabinoids are nearly insoluble in water but are soluble in lipids, alcohols, and other non-polar organic solvents. However, as phenols, they form more water-soluble phenolate salts under strongly alkaline conditions.

All-natural cannabinoids are derived from their respective 2-carboxylic acids (2-COOH) by decarboxylation (catalyzed by heat, light, or alkaline conditions).

Types

At least 85 different cannabinoids have been isolated from the *Cannabis* plant.[11] At least 25 different cannabinoids have been isolated from *Echinacea* species.[12] To the right, the main classes of cannabinoids from *Cannabis* are shown. All classes derive from cannabigerol-type compounds and differ mainly in the way this precursor is cyclized.

Tetrahydrocannabinol (THC), cannabidiol (CBD), cannabinol (CBN), and Dodeca-2E,4E,8Z,10E/Z-tetraenoic-acid-isobutylamides (from *Echinacea* species) are the most prevalent natural cannabinoids and have received the most study. Other common cannabinoids are listed below:

- CBG Cannabigerol
- CBC Cannabichromene
- CBL Cannabicyclol
- CBV Cannabivarin
- THCV Tetrahydrocannabivarin

- CBDV Cannabidivarin
- CBCV Cannabichromevarin
- CBGV Cannabigerovarin
- CBGM Cannabigerol Monomethyl Ether

Tetrahydrocannabinol

Tetrahydrocannabinol (THC) is the primary psychoactive component of the plant. It appears to ease moderate pain (analgesic) and to be neuroprotective. THC has approximately equal affinity for the CB_1 and CB_2 receptors.[13]

Delta-9-Tetrahydrocannabinol (Δ^9-THC, THC) and *delta*-8-tetrahydrocannabinol (Δ^8-THC), mimic the action of anandamide, a neurotransmitter produced naturally in the body. These two THC's produce the effects associated with cannabis by binding to the CB_1 cannabinoid receptors in the brain.

Cannabidiol

Cannabidiol (CBD) is not particularly psychoactive in and of itself, and was thought not to affect the psychoactivity of THC.[14] However, recent evidence shows that smokers of cannabis with a higher CBD/THC ratio were less likely to experience schizophrenia-like symptoms.[15] This is supported by psychological tests, in which participants experience less intense psychotic-like effects when intravenous THC was co-administered with CBD (as measured with a PANSS test).[16] Cannabidiol has little affinity for CB_1 and CB_2 receptors but acts as an indirect antagonist of cannabinoid agonists.[17] Recently it was found to be an antagonist at the putative new cannabinoid receptor, GPR55, a GPCR expressed in the caudate nucleus and putamen.[18] Cannabidiol has also been shown to act as a $5\text{-}HT_{1A}$ receptor agonist,[19] an action that is involved in its antidepressant,[20][21] anxiolytic,[21][22] and neuroprotective[23][24] effects.

It appears to relieve convulsion, inflammation, anxiety, and nausea.[25] CBD has a greater affinity for the CB_2 receptor than for the CB_1 receptor.[25]

CBD shares a precursor with THC and is the main cannabinoid in low-THC *Cannabis* strains. CBD apparently plays a role in preventing the short-term memory loss associated with THC in mammals.

Cannabinol

Cannabinol (CBN) is the primary product of THC degradation, and there is usually little of it in a fresh plant. CBN content increases as THC degrades in storage, and with exposure to light and air. It is only mildly psychoactive. Its affinity to the CB_2 receptor is higher than for the CB_1 receptor.[26]

Cannabigerol

Cannabigerol (CBG) is non-psychotomimetic but still affects the overall effects of Cannabis. It acts as an α_2-adrenergic receptor agonist, $5\text{-}HT_{1A}$ receptor antagonist, and CB_1 receptor antagonist.[27] It also binds to the CB_2 receptor.[27]

Tetrahydrocannabivarin

Tetrahydrocannabivarin (THCV) is prevalent in certain central Asian and southern African strains of *Cannabis*.[28] [29] It is an antagonist of THC at CB_1 receptors and attenuates the psychoactive effects of THC.[30]

Cannabidivarin

Although cannabidivarin (CBDV) is usually a minor constituent of the cannabinoid profile, enhanced levels of CBDV have been reported in feral plants from the northwest Himalayas, and in hashish from Nepal. [31][29]

Cannabichromene

Cannabichromene (CBC) is non-psychoactive and does not affect the psychoactivity of THC .[14]

Double bond position

In addition, each of the compounds above may be in different forms depending on the position of the double bond in the alicyclic carbon ring. There is potential for confusion because there are different numbering systems used to describe the position of this double bond. Under the dibenzopyran numbering system widely used today, the major form of THC is called Δ^9-THC, while the minor form is called Δ^8-THC. Under the alternate terpene numbering system, these same compounds are called Δ^1-THC and Δ^6-THC, respectively.

Length

Most herbal cannabinoid compounds are 21-carbon compounds. However, some do not follow this rule, primarily because of variation in the length of the side-chain attached to the aromatic ring. In THC, CBD, and CBN, this side-chain is a pentyl (5-carbon) chain. In the most common homologue, the pentyl chain is replaced with a propyl (3-carbon) chain. Cannabinoids with the propyl side-chain are named using the suffix *varin*, and are designated, for example, THCV, CBDV, or CBNV.

Plant profile

Cannabis plants can exhibit wide variation in the quantity and type of cannabinoids they produce. The mixture of cannabinoids produced by a plant is known as the plant's cannabinoid profile. Selective breeding has been used to control the genetics of plants and modify the cannabinoid profile. For example, strains that are used as fiber (commonly called hemp) are bred such that they are low in psychoactive chemicals like THC. Strains used in medicine are often bred for high CBD content, and strains used for recreational purposes are usually bred for high THC content or for a specific chemical balance.

Quantitative analysis of a plant's cannabinoid profile is often determined by gas chromatography (GC), or more reliably by gas chromatography combined with mass spectrometry (GC/MS). Liquid chromatography (LC) techniques are also possible, and, unlike GC methods, can differentiate between the acid and neutral forms of the cannabinoids. There have been systematic attempts to monitor the cannabinoid profile of cannabis over time, but their accuracy is impeded by the illegal status of the plant in many countries.

Pharmacology

Cannabinoids can be administered by smoking, vaporizing, oral ingestion, transdermal patch, intravenous injection, sublingual absorption, or rectal suppository. Once in the body, most cannabinoids are metabolized in the liver, especially by cytochrome P450 mixed-function oxidases, mainly CYP 2C9. Thus supplementing with CYP 2C9 inhibitors leads to extended intoxication.

Some is also stored in fat in addition to being metabolized in liver. Δ^9-THC is metabolized to 11-hydroxy-Δ^9-THC, which is then metabolized to 9-carboxy-THC. Some cannabis metabolites can be detected in the body several weeks after administration. These metabolites are the chemicals recognized by common antibody-based "drug tests"; in the case of THC et al., these loads do not represent intoxication (compare to ethanol breath tests that measure instantaneous blood alcohol levels) but an integration of past consumption over an approximately month-long window.

Plant synthesis

Cannabinoid production starts when an enzyme causes geranyl pyrophosphate and olivetolic acid to combine and form CBG. Next, CBG is independently converted to either CBD or CBC by two separate synthase enzymes. CBD is then enzymatically cyclized to THC. For the propyl homologues (THCV, CBDV and CBNV), there is a similar pathway that is based on CBGV. (recent studies show that THC is not cyclized from CBD but rather directly from CBG. no experiment thus far has turned up an enzyme that converts CBD into THC although it is still hypothesized.)

Separation

Cannabinoids can be separated from the plant by extraction with organic solvents. Hydrocarbons and alcohols are often used as solvents. However, these solvents are flammable and many are toxic. Butane may be used, which evaporates extremely quickly. Supercritical solvent extraction with carbon dioxide is an alternative technique. Although this process requires high pressures (73 atmospheres or more), there is minimal risk of fire or toxicity, solvent removal is simple and efficient, and extract quality can be well controlled. Once extracted, cannabinoid blends can be separated into individual components using wiped film vacuum distillation or other distillation techniques. However, to produce high-purity cannabinoids, chemical synthesis or semisynthesis is generally required.

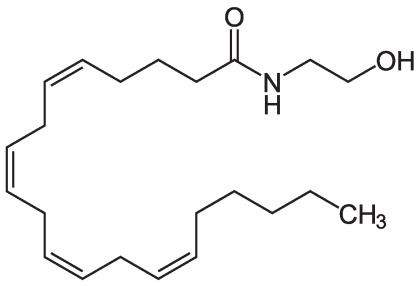
History

Cannabinoids were first discovered in the 1940s, when CBD and CBN were identified. The structure of THC was first determined in 1964.

Due to molecular similarity and ease of synthetic conversion, CBD was originally believed to be a natural precursor to THC. However, it is now known that CBD and THC are produced independently in the cannabis plant from the precursor CBG.

Endocannabinoids

Endocannabinoids are substances produced from within the body that activate cannabinoid receptors. After the discovery of the first cannabinoid receptor in 1988, scientists began searching for an endogenous ligand for the receptor.



Anandamide, an endogenous ligand of CB_1 and CB_2

Types of endocannabinoid ligands

- Arachidonoylethanolamine (Anandamide or AEA)

In 1992, in Raphael Mechoulam's lab, the first such compound was identified as arachidonoyl ethanolamine and named anandamide, a name derived from the Sanskrit word for bliss and *-amide*. Anandamide is derived from the essential fatty acid arachidonic acid. It has a pharmacology similar to THC, although its chemical structure is different. Anandamide binds to the central (CB_1) and, to a lesser extent, peripheral (CB_2) cannabinoid receptors, where it acts as a partial agonist. Anandamide is about as potent as THC at the CB_1 receptor.[32] Anandamide is found in nearly all tissues in a wide range of animals.[33] Anandamide has also been found in plants, including small amounts in chocolate.[34]

Two analogs of anandamide, 7,10,13,16-docosatetraenoylethanolamide and *homo*-γ-linolenoylethanolamine, have similar pharmacology. All of these are members of a family of signalling lipids called *N*-acylethanolamines, which also includes the noncannabimimetic palmitoylethanolamide and oleoylethanolamide, which possess anti-inflammatory and orexigenic effects, respectively. Many *N*-acylethanolamines have also been identified in plant seeds[35] and in molluscs.[36]

- 2-arachidonoyl glycerol (2-AG)

Another endocannabinoid, 2-arachidonoyl glycerol, binds to both the CB_1 and CB_2 receptors with similar affinity, acting as a full agonist at both.[32] 2-AG is present at significantly higher concentrations in the brain than anandamide,[37] and there is some controversy over whether 2-AG rather than anandamide is chiefly responsible for endocannabinoid signalling *in vivo*.[38] In particular, one *in vitro* study suggests that 2-AG is capable of stimulating higher G-protein activation than anandamide, although the physiological implications of this finding are not yet known.[39]

- 2-arachidonyl glyceryl ether (noladin ether)

In 2001, a third, ether-type endocannabinoid, 2-arachidonyl glyceryl ether (noladin ether), was isolated from porcine brain.[40] Prior to this discovery, it had been synthesized as a stable analog of 2-AG; indeed, some controversy remains over its classification as an endocannabinoid, as another group failed to detect the substance at "any appreciable amount" in the brains of several different mammalian species.[41] It binds to the CB_1 cannabinoid receptor (K_i = 21.2 nmol/L) and causes sedation, hypothermia, intestinal immobility, and mild antinociception in mice. It binds primarily to the CB_1 receptor, and only weakly to the CB_2 receptor.[32]

- N-arachidonoyl-dopamine (NADA)

Discovered in 2000, NADA preferentially binds to the CB_1 receptor.[42] Like anandamide, NADA is also an agonist for the vanilloid receptor subtype 1 (TRPV1), a member of the vanilloid receptor family.[43][44]

- Virodhamine (OAE)

A fifth endocannabinoid, virodhamine, or *O*-arachidonoyl-ethanolamine (OAE), was discovered in June 2002. Although it is a full agonist at CB_2 and a partial agonist at CB_1, it behaves as a CB_1 antagonist *in vivo*. In rats, virodhamine was found to be present at comparable or slightly lower concentrations than anandamide in the brain, but 2- to 9-fold higher concentrations peripherally.[45]

Function

Endocannabinoids serve as intercellular 'lipid messengers', signaling molecules that are released from one cell and activating the cannabinoid receptors present on other nearby cells. Although in this intercellular signaling role they are similar to the well-known monoamine neurotransmitters, such as acetylcholine and dopamine, endocannabinoids differ in numerous ways from them. For instance, they use retrograde signaling. Furthermore, endocannabinoids are lipophilic molecules that are not very soluble in water. They are not stored in vesicles, and exist as integral constituents of the membrane bilayers that make up cells. They are believed to be synthesized 'on-demand' rather than made and stored for later use. The mechanisms and enzymes underlying the biosynthesis of endocannabinoids remain elusive and continue to be an area of active research.

The endocannabinoid 2-AG has been found in bovine and human maternal milk.[46]

Retrograde signal

Conventional neurotransmitters are released from a ‘presynaptic’ cell and activate appropriate receptors on a ‘postsynaptic’ cell, where presynaptic and postsynaptic designate the sending and receiving sides of a synapse, respectively. Endocannabinoids, on the other hand, are described as retrograde transmitters because they most commonly travel ‘backward’ against the usual synaptic transmitter flow. They are, in effect, released from the postsynaptic cell and act on the presynaptic cell, where the target receptors are densely concentrated on axonal terminals in the zones from which conventional neurotransmitters are released. Activation of cannabinoid receptors temporarily reduces the amount of conventional neurotransmitter released. This endocannabinoid mediated system permits the postsynaptic cell to control its own incoming synaptic traffic. The ultimate effect on the endocannabinoid-releasing cell depends on the nature of the conventional transmitter being controlled. For instance, when the release of the inhibitory transmitter GABA is reduced, the net effect is an increase in the excitability of the endocannabinoid-releasing cell. On the converse, when release of the excitatory neurotransmitter glutamate is reduced, the net effect is a decrease in the excitability of the endocannabinoid-releasing cell.

Range

Endocannabinoids are hydrophobic molecules. They cannot travel unaided for long distances in the aqueous medium surrounding the cells from which they are released, and therefore act locally on nearby target cells. Hence, although emanating diffusely from their source cells, they have much more restricted spheres of influence than do hormones, which can affect cells throughout the body.

U.S. Patent no. 6630507

On October 7, 2003, a U.S. patent number 6630507 entitled "Cannabinoids as Antioxidants and Neuroprotectants" was awarded to the United States Department of Health and Human Services, based on research done at the National Institute of Mental Health (NIMH), and the National Institute of Neurological Disorders and Stroke (NINDS). This patent claims that cannabinoids are "useful in the treatment and prophylaxis of wide variety of oxidation associated diseases such as ischemia, age-related, inflammatory, and autoimmune diseases. The cannabinoids are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma, or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia."[47][48]

On November 17, 2011, in accordance with 35 U.S.C. 209(c)(1) and 37 CFR part 404.7(a)(1)(i), the National Institutes of Health, Department of Health and Human Services, published in the Federal Register, that it is contemplating the grant of an exclusive patent license to practice the invention embodied in U.S. Patent 6,630,507, entitled “Cannabinoids as antioxidants and neuroprotectants” and PCT Application Serial No. PCT/US99/08769 and foreign equivalents thereof, entitled “Cannabinoids as antioxidants and neuroprotectants” [HHS Ref. No. E-287-1997/2] to KannaLife Sciences Inc., which has offices in New York, U.S. This patent and its foreign

counterparts have been assigned to the Government of the United States of America. The prospective exclusive license territory may be worldwide, and the field of use may be limited to: The development and sale of cannabinoid(s) and cannabidiol(s) based therapeutics as antioxidants and neuroprotectants for use and delivery in humans, for the treatment of hepatic encephalopathy, as claimed in the Licensed Patent Rights.[49]

On June 12, 2012, KannaLife Sciences, Inc. signed an exclusive license agreement with National Institutes of Health – Office of Technology Transfer ("NIH-OTT") for the Commercialization of U.S. Patent 6,630,507, "Cannabinoids as Antioxidants and Neuroprotectants" (the "'507 Patent"). The '507 Patent includes among other things, claims directed to a method of treating diseases caused by oxidative stress by administering a therapeutically effective amount of a non-psychoactive cannabinoid that has substantially no binding to the NMDA receptor. Cannabinoids are any of a group of related compounds that include cannabinol and the active constituents of cannabis (marijuana).</ref>

Synthetic and patented cannabinoids

Historically, laboratory synthesis of cannabinoids were often based on the structure of herbal cannabinoids, and a large number of analogs have been produced and tested, especially in a group led by Roger Adams as early as 1941 and later in a group led by Raphael Mechoulam. Newer compounds are no longer related to natural cannabinoids or are based on the structure of the endogenous cannabinoids.

Synthetic cannabinoids are particularly useful in experiments to determine the relationship between the structure and activity of cannabinoid compounds, by making systematic, incremental modifications of cannabinoid molecules.

Medications containing natural or synthetic cannabinoids or cannabinoid analogs:

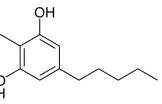
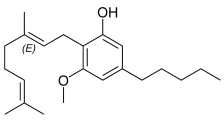
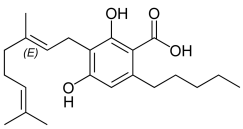
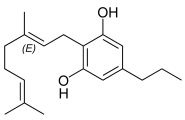
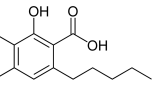
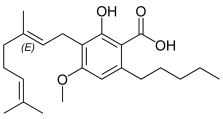
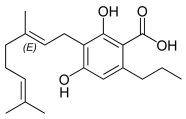
- Dronabinol (Marinol), is Δ^9-tetrahydrocannabinol (THC), used as an appetite stimulant, anti-emetic, and analgesic
- Nabilone (Cesamet), a synthetic cannabinoid and an analog of Marinol. It is Schedule II unlike Marinol, which is Schedule III
- Sativex, a cannabinoid extract oral spray containing THC, CBD, and other cannabinoids used for neuropathic pain and spasticity in 22 countries including England, Canada and Spain. Sativex develops whole-plant cannabinoid medicines
- Rimonabant (SR141716), a selective cannabinoid (CB_1) receptor inverse agonist used as an anti-obesity drug under the proprietary name Acomplia. It is also used for smoking cessation

Other notable synthetic cannabinoids include:

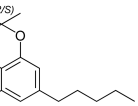
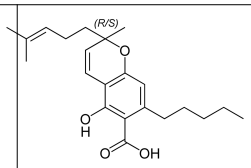
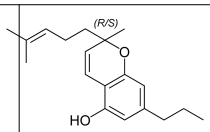
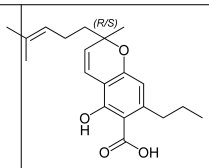
- JWH-018, a potent synthetic cannabinoid agonist discovered by Dr. John W. Huffman at Clemson University. It is being increasingly sold in legal smoke blends collectively known as "spice". Several countries and states have moved to ban it legally.
- CP-55940, produced in 1974, this synthetic cannabinoid receptor agonist is many times more potent than THC.
- Dimethylheptylpyran
- HU-210, about 100 times as potent as THC[50]
- HU-331 a potential anti-cancer drug derived from cannabidiol that specifically inhibits topoisomerase II.
- SR144528, a CB_2 receptor antagonist
- WIN 55,212-2, a potent cannabinoid receptor agonist
- JWH-133, a potent selective CB_2 receptor agonist
- Levonantradol (Nantrodolum), an anti-emetic and analgesic but not currently in use in medicine
- AM-2201, a potent cannabinoid receptor agonist.

Table of natural cannabinoids

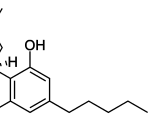
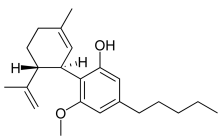
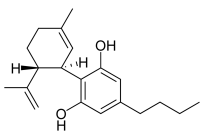
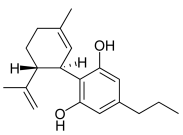
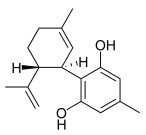
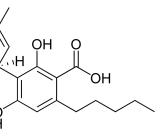
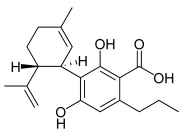
Cannabigerol-type (CBG)

 Cannabigerol **(*E*)-CBG-C_5**	 Cannabigerol monomethyl ether **(*E*)-CBGM-C_5A**	 Cannabinerolic acid A **(Z)-CBGA-C_5A**	 Cannabigerovarin **(*E*)-CBGV-C_3**	
 Cannabigerolic acid A **(*E*)-CBGA-C_5A**	 Cannabigerolic acid A monomethyl ether **(*E*)-CBGAM-C_5A**	 Cannabigerovarinic acid A **(*E*)-CBGVA-C_3A**		

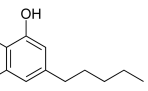
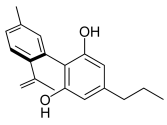
Cannabichromene-type (CBC)

 (±)-Cannabichr **CBC-C_5**	 (±)-Cannabichromenic acid A **CBCA-C_5A**	 (±)-Cannabivarichro (±)-Cannabichromevarin **CBCV-C_3**	 (±)-Cannabichromevarinic acid A **CBCVA-C_3A**	

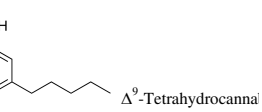
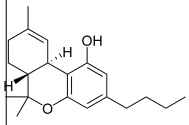
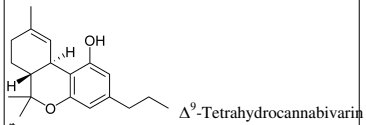
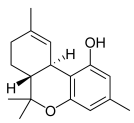
Cannabidiol-type (CBD)

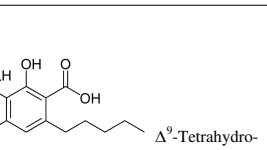
 (−)-Cannabidiol **CBD-C_5**	 Cannabidiol momomethyl ether **CBDM-C_5**	 Cannabidiol-C_4 **CBD-C_4**	 (−)-Cannabidivarin **CBDV-C_3**	 Cannabi **CBD-C_1**
 Cannabidiolic acid **CBDA-C_5**	 Cannabidivarinic acid **CBDVA-C_3**			

Cannabinodiol-type (CBND)

 Cannabinodiol **CBND-C_5**	 Cannabinodivarin **CBND-C_3**			

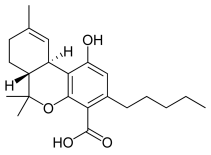
Tetrahydrocannabinol-type (THC)

 Δ^9-Tetrahydrocanna **Δ^9-THC-C_5**	 Δ^9-Tetrahydrocannabinol- **Δ^9-THC-C_4**	 Δ^9-Tetrahydrocannabivarin **Δ^9-THCV-C_3**	 Δ^9-Tetrahydrocannabiorcol **Δ^9-THCO-C_1**	



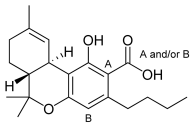
Δ⁹-Tetrahydrocannabinolic acid A

Δ⁹-THCA-C_5 A



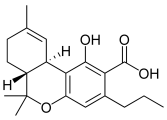
Δ⁹-Tetrahydrocannabinolic acid B

Δ⁹-THCA-C_5 B



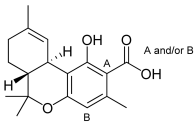
Δ⁹-Tetrahydrocannabinolic acid-C_4 A and/or B

Δ⁹-THCA-C_4 A and/or B



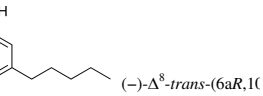
Δ⁹-Tetrahydrocannabivarinic acid A

Δ⁹-THCVA-C_3 A



Δ⁹-Tetrahydrocannabiorcolic acid A and/or B

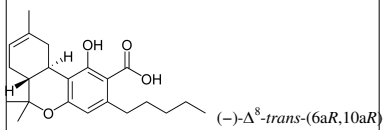
Δ⁹-THCOA-C_1 A and/or



(−)-Δ⁸-*trans*-(6a*R*,10

Δ⁸-Tetrahydrocannabinol

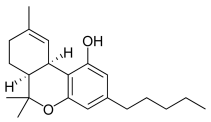
Δ⁸-THC-C_5



(−)-Δ⁸-*trans*-(6a*R*,10a*R*)-

Tetrahydrocannabinolic acid A

Δ⁸-THCA-C_5 A

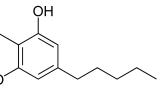


(−)-(6a*S*,10a*R*)-Δ⁹-

Tetrahydrocannabinol

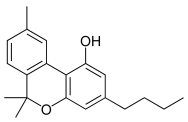
(−)-*cis*-Δ⁹-THC-C_5

Cannabinol-type (CBN)



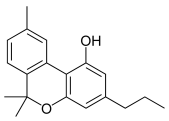
Cannabinol

CBN-C_5



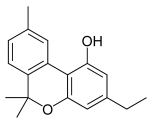
Cannabinol-C_4

CBN-C_4



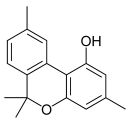
Cannabivarin

CBN-C_3



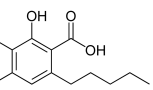
Cannabinol-C_2

CBN-C_2



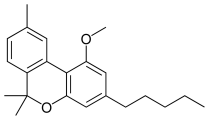
Cannabi

CBN-C_1



Cannabinolic acid A

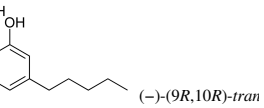
CBNA-C_5 A



Cannabinol methyl ether

CBNM-C_5

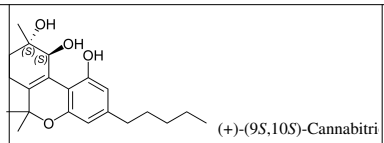
Cannabitriol-type (CBT)



(−)-(9*R*,10*R*)-*tran*

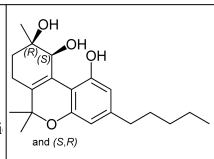
Cannabitriol

(−)-*trans*-CBT-C_5



(+)-(9*S*,10*S*)-Cannabitri

(+)-*trans*-CBT-C_5

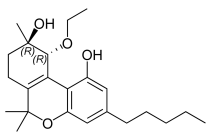


and (*S*,*R*)

(±)-(9*R*,10*S*/9*S*,10*R*)-

Cannabitriol

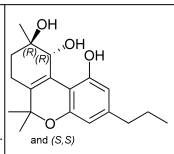
(±)-*cis*-CBT-C_5



(−)-(9*R*,10*R*)-*trans*-

10-O-Ethyl-cannabitriol

(−)-*trans*-CBT-OEt-C_5

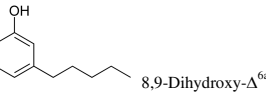


and (*S*,*S*)

(±)-(9*R*,10

Cannabitriol-C_3

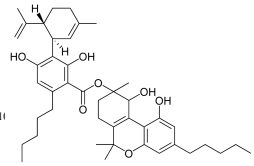
(±)-*trans*-CBT-C_3



8,9-Dihydroxy-Δ⁶ᵃ⁽¹⁰

tetrahydrocannabinol

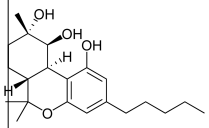
8,9-Di-OH-CBT-C_5



Cannabidiolic acid A

cannabitriol ester

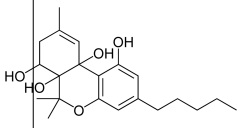
CBDA-C_5 9-OH-CBT-C_5 ester



(−)-(6a*R*,9*S*,10*S*,

9,10-Dihydroxy-hexahydrocannabinol, Cannabiripsol

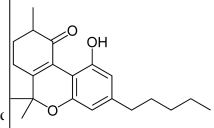
Cannabiripsol-C_5



(−)-6a,7,10a-Trihyd

Δ⁹-tetrahydrocannabinol

(−)-Cannabitetrol



10-(

tetrahydrocannabinol

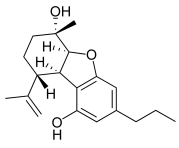
OTHC

Cannabielsoin-type (CBE)

(5a*S*,6*S*,9*R*,9a*R*)-

Cannabielsoin

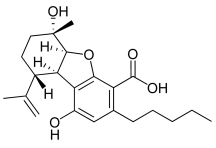
CBE-C_5



(5a*S*,6*S*,9*R*,9a*R*)-

C_3-Cannabielsoin

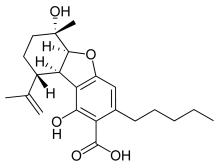
CBE-C_3



(5a*S*,6*S*,9*R*,9a*R*)-

Cannabielsoic acid A

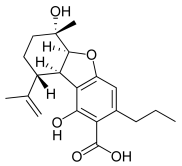
CBEA-C_5 A



(5a*S*,6*S*,9*R*,9a*R*)-

Cannabielsoic acid B

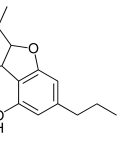
CBEA-C_5 B

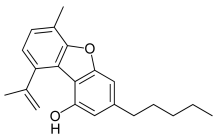


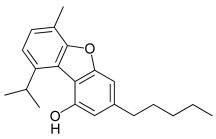
(5a*S*,6*S*

C_3-Cannabielsoic acid B

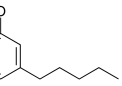
CBEA-C_3 B

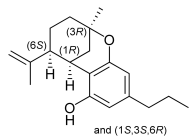

Cannabiglendol-C_3
OH-iso-HHCV-C_3

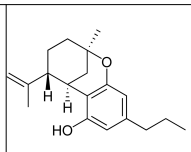

Dehydrocannabifuran
DCBF-C_5


Cannabifuran
CBF-C_5

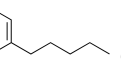
Isocannabinoids

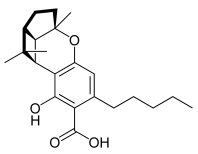

(−)-Δ^7-*trans*-(1*R*,3*R*,6*R*)-
Isotetrahydrocannabinol

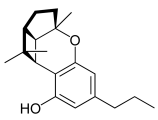

and (1*S*,3*S*,6*R*)
(±)-Δ^7-1,2-*cis*-
(1*R*,3*R*,6*S*/1*S*,3*S*,6*R*)-
Isotetrahydro-
cannabivarin


(−)-Δ^7-*trans*-(1*R*,3*R*,6*R*)-
Isotetrahydrocannabivarin

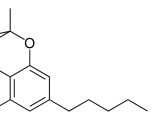
Cannabicyclol-type (CBL)


(±)-(1a*S*,3a*R*,8b*R*,8c*R*)-
Cannabicyclol
CBL-C_5

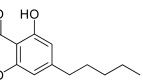

(±)-(1a*S*,3a*R*,8b*R*,8c*R*)-
Cannabicyclolic acid A
CBLA-C_5 A

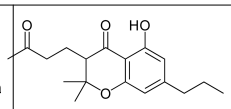

(±)-(1a*S*,3a*R*,8b*R*,8c*R*)-
Cannabicyclovarin
CBLV-C_3

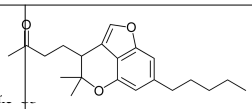
Cannabicitran-type (CBT)


Cannabicitran
CBT-C_5

Cannabichromanone-type (CBCN)


Cannabichroma
CBCN-C_5


Cannabichromanor...
CBCN-C_3


Cannabicoumaronone
CBCON-C_5

Natural occurrence

Cannabis indica may have a CBD:THC ratio 4–5 times that of *Cannabis sativa*. Cannabis strains with relatively high CBD:THC ratios are less likely to induce anxiety than vice versa. This may be due to CBD's antagonistic effects at the cannabinoid receptors, compared to THC's partial agonist effect. CBD is also a 5-HT_{1A} receptor agonist, which may also contribute to an anxiolytic effect.[51] This likely means the high concentrations of CBD found in *Cannabis indica* mitigate the anxiogenic effect of THC significantly.[51] The effects of *sativa* are well known for its cerebral high, hence used daytime as medical cannabis, while *indica* are well known for its sedative effects and preferred night time as medical cannabis.[51]

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The bud of a *Cannabis indica* flower coated with trichomes, which may contain 4-5 times more CBD than *Cannabis sativa*

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External links

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- Chemical Ecology of Cannabis (J. Intl. Hemp Assn. - 1994) (http://www.hempfood.com/IHA/iha01201.html)
- THC (tetrahydrocannabinol) accumulation in glands of Cannabis (Cannabaceae) (http://www.hempreport.com/issues/17/malbody17.html)

Cannabinoid research organizations

- The International Cannabinoid Research Society (http://www.cannabinoidsociety.org)
- The Canadian Consortium for the Investigation of Cannabinoids (http://www.ccic.net)
- Therapeutic Potential in Spotlight at Cannabinoid Researchers' Meeting (http://www.ccrmg.org/journal/04spr/potential.html) at California Cannabis Research Medical Group
- International Cannabinoid Research Society (http://cannabinoidsociety.org/)

Anticarcinogen

An **anticarcinogen** is any chemical which reduces the occurrence of cancers, reduces the severity of cancers that do occur, or acts against cancers that do occur, based on evidence from *in vitro* studies, animal models, epidemiological studies and/or clinical studies.

Preventative anticarcinogens act by enhancing an organism's natural defenses against cancer, by deactivating carcinogens or by blocking the mechanisms by which carcinogens act (such as free radical damage to DNA).

Anticarcinoma agents participate in the selective destruction of cancer cells, or inhibit the growth and proliferation of cancer cells. *See also: Chemotherapy.*

Interest in preventative anticarcinogens is motivated primarily by the principle that it is preferable to prevent disease where possible, and that positive actions can be effective as well as negative ones (such as reducing exposure to known carcinogens). Anticarcinoma agents that do not have significant negative side effects have a similar potential role, by reducing the seriousness of any cancers that do occur.

Known anticarcinogens

There is epidemiological evidence that a diet rich in antioxidant vitamins and flavonoids is anticarcinogenic. Interest in many popular nutritional supplements, including essential antioxidant nutrients such as selenium compounds and hormones such as melatonin and DHEA, is partly motivated by evidence that these have significant anticarcinogenic effects in appropriate quantities. The major psychoactive component in marijuana, tetrahydrocannabinol, has been shown to have anticarcinogenic activity, when injected into mice.[1] The other major component of cannabis - cannabidiol, has also been shown to inhibit cancer cell growth, with low potency in non-cancer cells. Although the inhibitory mechanism is not yet fully understood, Ligresti et al. suggest that "cannabidiol exerts its effects on these cells through a combination of mechanisms that include either direct or indirect activation of CB_2 and TRPV1

receptors, and induction of oxidative stress, all contributing to induce apoptosis.".[2]

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Hortapharm B.V.

Hortapharm B.V.

Industry	Horticulture
Founder(s)	David Paul Watson
Headquarters	Amsterdam, Netherlands [1]
Products	Cannabis based medicine extracts

Hortapharm B.V. is a major cannabis research and development business, based in the Netherlands.[2]

History

Founded by two expert horticulturists from California, Robert Connell Clarke [3] and David Paul Watson [4] who is also known as the "Skunkman".

They obtained a permit from the US Drug Enforcement Administration (DEA) to build several registered controlled substance research facilities in Europe to grow hundreds of tons of legal Cannabis. [5] [6] [7]

Today Hortapharm B.V. has a partnership with GW Pharmaceuticals to cultivates raw cannabis material for the manufacture of pharmaceuticals.[8]

Breeding

Using selective breeding and production control, Hortapharm created Cannabis strains that could hold single cannabinoids, with only 99% THC or 99% cannabidiol.[9]

Patents

The Cannabis plant cannot be patented because it is a natural product, however under the United States patent law companies that develop new cannabis strains that are not found on the nature can be patented.

- Cannabis Sativa plants rich in Cannabi Chromene and its acid, extracts thereof and methods of obtaining extracts therefrom.[10]
- Enhanced isolation chambers for ascending-stream extractive vaporizer [11]
- Skunk #1

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[3] https://www.google.ca/search?tbo=p&tbm=bks&q=inauthor:%22Robert+Connell+Clarke%22
[4] http://fourtwentywiki.com/sam-the-skunkman
[5] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2736886/pdf/erp210.pdf Seeds from the marijuana cultivar Skunk no. 1 were provided by HortaPharm BV (Amsterdam, The Netherlands) and imported under a US Drug Enforcement Administration (DEA) permit to a registered controlled substance research facility.
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